



Year: 2021

Cariogenic potential of oral nutritional supplements measured by intraoral plaque pH telemetry

Stillhart, Angela ; Wegehaupt, Florian J ; Nitschke, Ina ; Attin, Thomas ; Srinivasan, Murali

Abstract: Background aims Oral nutritional supplements (ONS) administered to malnourished elders and other patients contain high-levels of carbohydrates that could be a potential risk factor for dental caries. This study aimed to evaluate the cariogenic potentials of ONS using intraoral plaque telemetry. Methods Ten ONS were tested on five healthy volunteers (mean age: 76.8 ± 9.15 years). Participants were requested to refrain from performing oral hygiene 3–7 days prior to testing. The pH-value below the dental plaque on the tooth was measured while the ONS was being consumed. After neutralizing the participant's saliva, a control solution (10% sucrose) was administered and telemetry measurements were repeated. Mean relative cariogenicity (RC) was calculated for each ONS. ANOVA and post hoc tests were used for statistical analyses ($p < 0.05$). Results All ten ONS were potentially cariogenic on enamel with an overall RC of 0.519 ± 0.35 (Range: Min = 0.31 ± 0.16 ; Max = 1.00 ± 0.34). RC differed significantly between the ONS ($p = 0.002$). RC was lower in ONS that contained high-protein ($p = 0.018$). RC was not influenced by other factors such as readily consumable ($p = 0.102$), flavor ($p = 0.869$), consistency ($p = 0.126$), fiber containing ($p = 0.134$), style ($p = 0.112$), and age of plaque ($p = 0.339$). Conclusions The ONS administered to elders and malnourished patients are potentially cariogenic. It is imperative that the administration of ONS must be based on individual needs to potentiate a maximum benefit. Wherever possible, an attempt to limit the use of high-carbohydrate containing ONS must be practiced along with the adoption of suitable preventive measures to arrest the development and progression of caries.

DOI: <https://doi.org/10.1016/j.clnu.2020.11.026>

Posted at the Zurich Open Repository and Archive, University of Zurich

ZORA URL: <https://doi.org/10.5167/uzh-195611>

Journal Article

Published Version



The following work is licensed under a Creative Commons: Attribution 4.0 International (CC BY 4.0) License.

Originally published at:

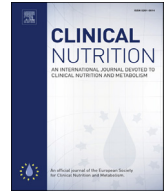
Stillhart, Angela; Wegehaupt, Florian J; Nitschke, Ina; Attin, Thomas; Srinivasan, Murali (2021). Cariogenic potential of oral nutritional supplements measured by intraoral plaque pH telemetry. *Clinical Nutrition*, 40(5):3448-3453.

DOI: <https://doi.org/10.1016/j.clnu.2020.11.026>



Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: <http://www.elsevier.com/locate/clnu>

Original article

Cariogenic potential of oral nutritional supplements measured by intraoral plaque pH telemetry

Angela Stillhart^{a,*}, Florian J. Wegehaupt^b, Ina Nitschke^a, Thomas Attin^b,
Murali Srinivasan^a^a Clinic of General, Special Care and Geriatric Dentistry, Center of Dental Medicine, University of Zurich, Zurich, Switzerland^b Clinic of Conservative and Preventive Dentistry, Center of Dental Medicine, University Zurich, Zurich, Switzerland

ARTICLE INFO

Article history:

Received 24 June 2020

Accepted 20 November 2020

Keywords:

Oral nutritional supplements

Dental caries

Oral hygiene

Malnutrition

Caries risk

pH telemetry

SUMMARY

Background & aims: Oral nutritional supplements (ONS) administered to malnourished elders and other patients contain high-levels of carbohydrates that could be a potential risk factor for dental caries. This study aimed to evaluate the cariogenic potentials of ONS using intraoral plaque telemetry.

Methods: Ten ONS were tested on five healthy volunteers (mean age: 76.8 ± 9.15 years). Participants were requested to refrain from performing oral hygiene 3–7 days prior to testing. The pH-value below the dental plaque on the tooth was measured while the ONS was being consumed. After neutralizing the participant's saliva, a control solution (10% sucrose) was administered and telemetry measurements were repeated. Mean relative cariogenicity (RC) was calculated for each ONS. ANOVA and post hoc tests were used for statistical analyses ($p < 0.05$).

Results: All ten ONS were potentially cariogenic on enamel with an overall RC of 0.519 ± 0.35 (Range: Min = 0.31 ± 0.16 ; Max = 1.00 ± 0.34). RC differed significantly between the ONS ($p = 0.002$). RC was lower in ONS that contained high-protein ($p = 0.018$). RC was not influenced by other factors such as readily consumable ($p = 0.102$), flavor ($p = 0.869$), consistency ($p = 0.126$), fiber containing ($p = 0.134$), style ($p = 0.112$), and age of plaque ($p = 0.339$).

Conclusions: The ONS administered to elders and malnourished patients are potentially cariogenic. It is imperative that the administration of ONS must be based on individual needs to potentiate a maximum benefit. Wherever possible, an attempt to limit the use of high-carbohydrate containing ONS must be practiced along with the adoption of suitable preventive measures to arrest the development and progression of caries.

© 2020 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Oral nutritional supplements (ONS) are administered to malnourished patients as well as frail, care-dependent elders in different health care settings to reduce the burden of malnutrition, strengthen function, and improve their quality of life [1]. These supplements usually contain high levels of carbohydrates, amongst other essential constituents, which counter malnutrition. The current global population demographic trends suggest that the elderly population is increasing [2,3], and in developed nations teeth are

being retained to an advanced age [4–6]. Tooth loss in adults has been associated with an impairment of the Oral Health-Related Quality of Life (OHRQoL), and the distribution of tooth loss affects the severity of the impairment [7]. Hence, preventive strategies to avoid tooth loss in elders is considered imperative.

It is essential to identify the carbohydrate-content in foods for the purpose of caries prevention [8]. Exposure of oral bacteria to fermentable carbohydrates leads to the production of organic acids [9,10]. Organic acids are known to decrease oral pH, initiating caries development at a critical pH value [9]. Research indicates that, compared to a carbohydrate-free diet [10], a carbohydrate-rich diet leads to a rapid pH decrease in plaque, which disturbs the equilibrium between the calcium and phosphate concentration in the enamel hydroxyapatite and plaque [9]. *In-vitro*-studies have demonstrated the initiation of demineralization of enamel was at pH < 5.5 [11], and of radicular dentine at pH < 6.7 [12].

* Corresponding author. Clinic of General, Special Care and Geriatric Dentistry, Center of Dental Medicine, University of Zurich, Zurich, Switzerland. Fax: +41 44 634 43 19.

E-mail address: angela.stillhart@zzm.uzh.ch (A. Stillhart).

Foodstuffs such as honey, sweets, beverages or drinking solutions, and pharmaceuticals have already been tested many years ago using the telemetry method, in order to prevent caries in the general population by means of education and product labeling (e.g. safe for teeth label) [13]. Even infant formulations have been identified to be highly cariogenic and potentially initiating early childhood caries [14]. However, industrially-manufactured ONS or senior formulas (Table 1) do not provide any information on their potential cariogenicity. Little or no evidence exists neither in experimental models nor in epidemiological studies on the cariogenicity of these products [15]. This is important, as dental caries, mainly root caries, is known to pose a major problem in geriatric patients [16]; and ONS are widely used in the treatment of malnutrition in this vulnerable group [17], especially in care-dependent institutionalized elders with dementia [18].

The elderly population is increasing worldwide, and people aged over 80 years old are projected to increase to approximately 426 million by 2050 [3]. Along with this trend, an increase in the number of teeth retained to an advanced age has also been reported [4–6]. Although, retention of teeth in older adults is a positive trend, nevertheless it also augments the risk for caries or root caries and their associated complications [19,20]. Root caries is a common clinical finding in dependent older adults and is estimated that approximately 39% of institutionalized elders are affected [20,21]. Caries-related complications may include acute pain [22], which can be undiagnosed in elders with severe dementia. Furthermore, untreated deep caries lesions may lead to pulpal necrosis and abscesses, which may have serious adverse effects in dependent elders. Caries accounts for tooth loss which occurs later in life [23–26]; tooth loss coupled with malnutrition and other pre-existing medical conditions can further affect the general health and oral health-related Quality of life of the elders [27]. Moreover, clinical procedures to treat these conditions in dependent older adults are complex and are often associated with increased medical risks, administrative, as well as financial challenges [28]. Therefore, prevention of caries and root caries in older adults is cardinal in safeguarding oral health.

This study aimed to quantify the caries potential of randomly selected ONS products frequently administered in Switzerland and to compare it against a standard known cariogenic (10%-sucrose solution) [26]. The null hypothesis of this study was that the tested ONS products have no cariogenic potential.

2. Materials and methods

The study procedure received ethics approval (KEK-ZH-No. StV 02/14). The tested ONS are classified in Switzerland as Foods for Special Medical Purposes (FSMP) by the national Federal Office of Public Health (FOPH).

Ten ONS formulations were randomly selected and purchased from the local pharmacies as over-the-counter-products (OTCs) which included, Cubitan® (N.V. Nutricia, Zoetermeer, The Netherlands), Fortimel Energy® (N.V. Nutricia, Zoetermeer, The Netherlands), Fresubin Energy Drink® (Fresenius Kabi Deutschland GmbH, Bad Homburg, Germany), Fortimel Jucy® (N.V. Nutricia, Zoetermeer, The Netherlands), Resource® 2.0 plus fibre (Nestlé S.A., Vevey, Switzerland), Calshake® (Fresenius Kabi Deutschland GmbH, Bad Homburg, Germany), Resource® Complete HP Shake (Nestlé S.A., Vevey, Switzerland), Resource® Dessert Cup Crème (Nestlé S.A., Vevey, Switzerland), Fortimel Fruit® (N.V. Nutricia, Zoetermeer, The Netherlands), Nutilis Complete® (N.V. Nutricia, Zoetermeer, The Netherlands). The listed ONS were available either as ready to consume or as a powder-milk formulation that were prepared according to the manufacturer's instructions for the tests.

This *in-vivo*-study was performed under standard laboratory test conditions in one of the internationally recognized and calibrated test centers [13]. The degree of the potential cariogenic pH attack on enamel in pH x min was obtained using a validated telemetric measurement series of the pH of interdental plaque and fluid. These measurements were recorded with the ONS and a standard control (10% sucrose solution) [13]. An oral washout procedure was performed by requesting the participants to rinse with water in between the test and control measurements. Clinical relevance for tooth demineralization was set at pH < 5.7 (critical pH for enamel). Area-under-the-curve (AuC) for pH < 5.7 for the ONS $AuC^P_{pH<5.7}$ and for the control sucrose solution, $AuC^S_{pH<5.7}$ were plotted. Relative cariogenicity (RC) potential was calculated using the formula $RC = AuC^P_{pH<5.7}/AuC^S_{pH<5.7}$.

The test assessed the hydrogen ion concentration (H^+) under an undisturbed layer of plaque at the level of the enamel surface on the teeth. Habitual consumption or normal diffusion of substrates into the interdental areas and in plaque were not disturbed during the continuous pH measurements [29]. This method is a standard procedure applied for testing foods, beverages, snacks, and medicines [13]. The specification of the internationally standardized

Table 1

Relative cariogenicities of the various oral nutritional supplement (ONS) products tested with 95%-confidence interval (95%-CI) and significance set at $p < 0.05$ (ANOVA) and RC influencing factors.

ONS Product	Flavor	Type	$AuC^P_{pH<5.7}$ (pH x Min) Mean \pm SD	$AuC^S_{pH<5.7}$ (pH x Min) Mean \pm SD	Relative Cariogenicity (AuC^P/AuC^S) Mean \pm SD, [95%-CI]
Fortimel Jucy	Fruit	RU, FB, HE	30.57 \pm 14.03	30.38 \pm 11.95	1.00 \pm 0.34, [0.4613, 1.5387]
Fortimel Energy	Other	RU, MB, HE	18.44 \pm 5.73	20.48 \pm 9.35	0.98 \pm 0.32, [0.4763, 1.4837]
Cubitan	Other	RU, MB, HE, HP	12.41 \pm 6.40	20.30 \pm 11.68	0.64 \pm 0.17, [0.3777, 0.9073]
Nutilis Complete	Fruit	RU, MB, HE, FE	11.56 \pm 8.95	23.09 \pm 7.52	0.48 \pm 0.24, [0.0966, 0.8634]
Fresubin Energy	Other	RU, MB, HE	8.85 \pm 4.27	22.88 \pm 6.64	0.41 \pm 0.21, [0.0772, 0.7328]
Fortimel Fruit	Fruit	RU, FB, SS, HE, HP, FE	9.31 \pm 10.39	18.20 \pm 9.91	0.39 \pm 0.30, [-0.0854, 0.8654]
Calshake	Fruit	MU, MB, HE	10.27 \pm 12.15	24.12 \pm 5.46	0.37 \pm 0.45, [-0.3516, 1.0916]
Resource 2.0 fibre	Other	RU, MB, HE, FE, HP	7.39 \pm 5.20	21.65 \pm 6.93	0.31 \pm 0.14, [0.0786, 0.5364]
Resource Complete	Other	MU, MB, HP	6.63 \pm 4.15	19.84 \pm 4.48	0.31 \pm 0.18, [0.0148, 0.6002]
Resource Dessert	Fruit	RU, MB, SS, HE, HP	6.02 \pm 4.34	18.19 \pm 7.19	0.31 \pm 0.16, [0.0567, 0.5633]
p-value (ANOVA)			0.008*	0.692	0.002*
RC influencing factors	protein content of the products [$F(1, 38) = 6.075$, $p = 0.018$], readily consumable [$F(1, 38) = 2.807$, $p = 0.102$], flavor [$F(1, 38) = 0.027$, $p = 0.869$], consistency [$F(1, 38) = 2.446$, $p = 0.126$], fiber containing [$F(1, 38) = 1.307$, $p = 0.134$], style [$F(1, 38) = 2.651$, $p = 0.112$], age of plaque [$F(3, 36) = 1.157$, $p = 0.339$].				

RU – Ready to use; FB – Fruit-based; HE – High-energy; MB – Milk-based; HP – High-Protein; FE – Fiber-enriched; SS – Semi-solid; MU – Mix and use; $AuC^P_{pH<5.7}$ – Area under the curve for ONS for pH < 5.7; $AuC^S_{pH<5.7}$ – Area under the curve for 10%-sucrose for pH < 5.7; SD – Standard deviation; * – significant ($p < 0.05$). Note: RC 1.00 = 100% as cariogenic as 10%-sucrose solution, RC 0.50 = 50% cariogenicity.

study protocol for “safe for teeth” products, recommends four repeated measurements with at least two participants to guarantee reliability of the measurements [13].

A cariogenic potential of the tested product is given when the maximal interdental pH drop is below 5.7 (critical pH for potential enamel damage in tests) after consumption.

2.1. Study protocol

Five volunteers (2 men and 3 women; mean age: 76.8 ± 9.15 years) were enrolled from the volunteer pool of the telemetry center in the Clinic of Conservative and Preventive Dentistry, Center of Dental Medicine at the University of Zurich in Switzerland. An informed consent was received from all participants. These participants were included if they satisfied the following inclusion criteria:

- missing teeth in the premolar and molar regions of the mandible,
- no active caries lesions,
- no untreated caries cavities, periodontal or other oral diseases,
- stimulated salivary secretion rate >0.6 ml/min [30] measured by the collection of whole saliva after chewing an inert gum base for 5 min,
- wearing a removable partial denture,
- no medications in medical records.

A test electrode in a partial denture, specially fabricated for each test subject, served to record the plaque-pH values measured for 30 min graphically and numerically. The measuring electrodes were installed interdentally distal to the canine tooth or the first or second premolar [31]. The tests were performed in a laboratory, which frequently performs such experiments for the industry in order to get the product certification “safe for teeth” [13]. The tests were sequenced and timed as described in a previously published similar experiment [29]. The participants were requested to refrain from toothbrushing and other oral hygiene procedures for at least 3–7 days before the testing, in order to allow sufficient biofilm (dental plaque) build up [13]. A reference electrode was placed on the right forearm. A measuring electrode was built in the respective partial dentures that were connected to a data recorder (Fig. 1). To neutralize the oral fluid the participants were requested to chew on paraffin wax for approximately 2–3 minutes (Fig. 2, pc). The participants were then administered the ONS (Fig. 2, t) at room temperature and requested to maintain the solution in the mouth for 2 minutes. The telemetric pH measurements were then



Fig. 1. Telemetry volunteer with a specially manufactured removable partial denture in the mouth that is connected by a wire to the recording equipment.

recorded for 30 minutes. A wash-out procedure was performed by serving the participants a rinse with water to neutralize the pH value (Fig. 2, w). The participants were requested to chew on paraffin again to produce neutral saliva. Following this the control solution (10%-sugar solution) was administered and the measuring procedures performed for the test solution were repeated to observe the functionality of the plaque (pH value must fall <5). The protocol allows one single test series (1 ONS and 1 control) per day. At the end of all tests, a dental hygiene procedure was carried out by a dental hygienist, which included prophylaxis along with a fluoride application on the participants' teeth.

Relative cariogenicity (RC) was expressed as a mean \pm standard deviation. Data was verified for a normal distribution. ANOVA and post hoc tests (LSD test) were used to evaluate the difference in the RC between the products with the level of statistical significance set at $p < 0.05$. Ancillary analyses included the effects of the characteristic of ONS such as readily consumable (ready to use or mix and use), flavor (fruit or other), age of plaque (3–7 days), consistency (semi-solid or liquid), fiber containing (fiber-enriched or regular), protein containing (high protein or regular) and style (milk-based or fruit-based) on the RC.

3. Results

The mean RC of the various tested ONS with 95% confidence interval (95% CI) is shown in Table 1, along with the characteristics and categorizations of the products. The $AuC^P_{pH<5.7}$ ranged between 6.02 ± 4.34 and 30.57 ± 14.03 (Table 1). Statistical analysis revealed a significant difference between the various tested products $AuC^P_{pH<5.7}$ [$F(9, 30) = 3.183, p = 0.008$]. All ONS tested showed a potential cariogenicity on enamel. Relative cariogenicity was shown to be between 0.31 ± 0.16 [95%-CI: 0.0567, 0.5633] and 1.00 ± 0.34 [95%-CI: 0.4613, 1.5387]. A significant difference between the RC of the different ONS [$F(9, 30) = 3.998, p = 0.002$] was demonstrated (Table 2.).

RC was lower in ONS that contained high protein [$F(1, 38) = 6.075, p = 0.018$]. Other factors such as readily consumable [$F(1, 38) = 2.807, p = 0.102$], flavor [$F(1, 38) = 0.027, p = 0.869$], consistency [$F(1, 38) = 2.446, p = 0.126$], fiber-containing [$F(1, 38) = 1.307, p = 0.134$], style [$F(1, 38) = 2.651, p = 0.112$], and age of plaque [$F(3, 36) = 1.157, p = 0.339$] did not influence the RC. All details of the ONS are shown in Table 1 and are listed according to the decreasing RC potentials.

4. Discussion

As this study provides clear evidence that all the tested ONS are potentially cariogenic on enamel, the null hypothesis is therefore rejected. It is apparent that the results are most germane to conditions in the mouth of elderly or other risk groups (e.g. oncology). Interventional epidemiological studies would most probably confirm this. Administration of these ONS pose serious ethical concerns. Variability in the results were observed between the participants. This could be because of a few factors. Firstly, this variability could be because of the constitution of the individual himself. Different individuals demonstrate different caries risk susceptibility [32]. Therefore, the potential cariogenic risk imposed by each ONS can be varied. Then there is the fact that only 5 volunteers were tested and the measurements were repeated only four times for each participant. This low number of repeated observations might have contributed to an amplified result. However, it has been demonstrated by previous published studies that the number of participants used and the number of repeated observations performed in the current study is an acceptable protocol for such experiments [13].

product information on the package and on the product-homepage was lacking. Hence, precise influences from processed foods, carbohydrates and other nutrients were not identifiable [45]. Although the study did demonstrate that the RC potentials of high-protein containing ONS containing were lower, it could not be ascertained why this was so. It can only be speculated, at this juncture, that the high-protein containing ONS will be beneficial in providing a protective effect of proteins for prevention of caries as demonstrated by previous studies [45]. This however, needs to be confirmed by future studies. A recommendation of a specific product is not possible from our results. However, we can recommend that the RC potentials of the ONS must be considered before administering it to the elder. The ONS indicated for a particular clinical situation must be weighed against other possible options, and the product with the lowest RC within the same category must be prescribed (e.g. Resource 2.0 fibre: lowest cariogenicity among high-energy, fiber-enriched, high-protein products; Table 1). Actual research on preventive fluoride supplementation (≥ 5 ppm sodium fluoride) in higher carbohydrate-containing ONS shows promising in-vitro results [33], which still needs to be confirmed in-vivo. Hence, the possibility for the consumers and prescribers to choose a less cariogenic product [43], or respective changes of the industrial formulations must be recommended. Moreover, the findings of this study emphasize that the products should be labeled to state whether they are “safe for teeth” or not [46].

The telemetry method used in our study is a standard for labeling products according to the criteria of Toothfriendly International as “safe for teeth”. There is no label for “not safe for teeth”, but there should be an explicit call for oral health safeguarding measures in ONS consumers. In 2009, authors from a special interest group [47] have assumed that ONS are cariogenic. Our results support their assumption. The interest group recommends a multidisciplinary community nutrition team approach, an Oral Health Risk Assessment, patient information leaflets, a caregiver training on the impact of ONS on dental health, strategies to improve nutritional intake from food, and oral nutrition integrated care pathways.

The current study has several strengths, including a control, use of a validated objective, and an internationally accredited tool assessing potential cariogenicity on enamel, utilization of a largely accepted standardized scientific procedure, which yields sufficient power to detect effects in healthy subjects. Limitations include the fact that we did not test the effects on a larger vulnerable caries risk population. Finally, these results do not give an in-depth analysis of which carbohydrate in the formulation contributed most to the cariogenic potential.

ONS are usually given to the patients in between meals. This could be a contributing effect for the cariogenic potential as demonstrated by the Vipeholm Study (1954) [35]. The study demonstrated that the effects of repeated intake of cariogenic food in-between meals, in vulnerable subjects, is a high risk factor for the development of caries [35]. Therefore, along with the carbohydrate content, it is equitably imperative on the close monitoring of the frequency and the time of the administration of the ONS along with an efficient oral hygiene plan. Furthermore, manufacturers are encouraged to provide information about the carbohydrate content on the packaging of their respective ONS in order to aid the consumer as well as the clinicians in planning adequate preventive and hygiene measures.

5. Conclusions

The ONS administered to the elders and malnourished patients are potentially cariogenic. It is imperative that the administration of the ONS must be based on individual needs to potentiate a

maximum benefit. Wherever possible, an attempt to limit the use of high-carbohydrate containing ONS must be practiced along with the adoption of suitable preventive measures to arrest the development and progression of dental caries.

Statement of authorship

Angela Stillhart: conceptualization, data curation, formal analysis, methodology, project administration, resources, visualization, roles/writing original draft.

Florian Wegehaupt: data curation, formal analysis, investigation, writing-review & editing.

Ina Nitschke: conceptualization, project administration, supervision, resources, writing-review & editing.

Thomas Attin: resources, funding acquisition, writing-review & editing.

Murali Srinivasan: resources, supervision, project administration, data curation, formal analysis, methodology, roles/writing original draft, visualization, writing-review & editing.

Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit-sectors.

Conflict of interest

AS, IN, TA, MS: declare no conflicts of interest.

FW: member of the board of Toothfriendly Switzerland.

Acknowledgements

The authors thank Prof. em. Dr. med. dent. Thomas Imfeld MBA for his expert help in the telemetry procedures conducted in this study.

References

- [1] Volkert D, Beck AM, Cederholm T, Cruz-Jentoft A, Goisser S, Hooper L, et al. ESPEN guideline on clinical nutrition and hydration in geriatrics. *Clin Nutr* 2019 Feb;38(1):10–47.
- [2] United Nations, Department of Economic and Social Affairs, Population Division. World population ageing 2019: highlights. ST/ESA/SER.A/430; 2019.
- [3] United Nations, Department of Economic and Social Affairs, Population Division. World population prospects 2019: highlights. ST/ESA/SER.A/423; 2019.
- [4] Schimmel M, Müller F, Suter V, Buser D. Implants for elderly patients. *Periodontol* 2017;73(1):228–40. 2000.
- [5] Schneider C, Zemp E, Zitzmann NU. Oral health improvements in Switzerland over 20 years. *Eur J Oral Sci* 2017;125(1):55–62.
- [6] Zitzmann NU, Staehelin K, Walls AWG, Menghini G, Weiger R, Stutz EZ. Changes in oral health over a 10-yr period in Switzerland. *Eur J Oral Sci* 2008;116(1):52–9.
- [7] Gerritsen AE, Allen PF, Witter DJ, Bronkhorst EM, Creugers NH. Tooth loss and oral health-related quality of life: a systematic review and meta-analysis. *Health Qual Life Outcome* 2010;8:126.
- [8] Moynihan P. Sugars and Dental Caries: evidence for setting a recommended threshold for intake. *Adv Nutr* 2016;7(1):149–56.
- [9] Stephan RM. Two factors of possible importance in relation to the etiology and treatment of dental caries and other dental diseases. *Science* 1940;92(2399): 578–9.
- [10] Sheiham A, James WP. Diet and dental caries: the pivotal role of free sugars reemphasized. *J Dent Res* 2015;94(10):1341–7.
- [11] Stephan RM. Intra-oral hydrogen-ion concentrations associated with dental caries activity. *J Dent Res* 1944;23(4):257–66.
- [12] Hoppenbrouwers PM, Driessens FC, Borggreven JM. The mineral solubility of human tooth roots. *Arch Oral Biol* 1987;32(5):319–22.
- [13] Toothfriendly Guidelines. pH-Telemetry testing. Measuring the cariogenic and erosive potential of foods and food ingredients. Toothfriendly International. 2015. https://www.toothfriendly.org/images/pHTelemetry_Guidelines.pdf. [Accessed 21 March 2020].
- [14] Tan SF, Tong HJ, Lin XY, Mok B, Hong CH. The cariogenicity of commercial infant formulas: a systematic review. *Eur Arch Paediatr Dent: Off J Eur Arch Paediatr Dent*. 2016;17(3):145–56.

- [15] Castro RJ, Giacaman RA, Arthur RA, Maltz M. Cariogenicity of a milk-based drink used as a dietary supplement for older adults using a root caries experimental model. *Carbohydr Res* 2019;53(1):76–83.
- [16] Petersen PE, Yamamoto T. Improving the oral health of older people: the approach of the WHO Global Oral Health Programme. *Community Dent Oral Epidemiol* 2005;33:81–92.
- [17] Streicher M, Themessl-Huber M, Schindler K, Sieber CC, Hiesmayr M, Volkert D. Who receives oral nutritional supplements in nursing homes? Results from the nutritionDay project. *Clin Nutr* 2017;36(5):1360–71.
- [18] Reuther S, van Nie N, Meijers J, Halfens R, Bartholomeyczik S. [Malnutrition and dementia in the elderly in German nursing homes. Results of a prevalence survey from the years 2008 and 2009]. *Z Gerontol Geriatr* 2013;46(3):260–7.
- [19] Gbd 2017 Oral Disorders Collaborators, Bernabé E, Marcenes W, Hernandez CR, Bailey J, Abreu LG, et al. Global, regional, and national levels and trends in burden of oral conditions from 1990 to 2017: a systematic analysis for the global burden of disease 2017 study. *J Dent Res* 2020 Apr;99(4):362–73.
- [20] Hayes M, Da Mata C, Cole M, McKenna G, Burke F, Allen PF. Risk indicators associated with root caries in independently living older adults. *J Dent* 2016;51:8–14.
- [21] Imazato S, Ikebe K, Nokubi T, Ebisu S, Walls AW. Prevalence of root caries in a selected population of older adults in Japan. *J Oral Rehabil* 2006;33(2):137–43.
- [22] Mayo Foundation for Medical Education and Research (MFMER) 70. Cavities/tooth decay [Internet]. 2020. <https://www.mayoclinic.org/diseases-conditions/cavities/symptoms-causes/syc-20352892>. [Accessed 1 October 2020].
- [23] Stock C, Jürges H, Shen J, Bozorgmehr K, Listl S. A comparison of tooth retention and replacement across 15 countries in the over-50s. *Community Dent Oral Epidemiol* 2016;44(3):223–31.
- [24] Hugoson A, Koch G, Gothberg C, Helkimo AN, Lundin SA, Norderyd O, et al. Oral health of individuals aged 3–80 years in Jonkoping, Sweden during 30 years (1973–2003). II. Review of clinical and radiographic findings. *Swed Dent J* 2005;29(4):139–55.
- [25] Jordan AR, Micheelis W. Fünfte deutsche mundgesundheitsstudie (DMS V). Fifth German oral health survey. Cologne: Deutscher Zahnärzteverlag Köln; 2016.
- [26] Hellwig E, Schäfer E, Klimek J, Attin T. Einführung in die Zahnerhaltung. 7th ed. Köln: Aerzte-Verlag; 2018.
- [27] Ruggiero SL, Dodson TB, Fantasia J, Goodday R, Aghaloo T, Mehrotra B, et al. American Association of Oral and Maxillofacial Surgeons position paper on medication-related osteonecrosis of the jaw - 2014 update. *J Oral Maxillofac Surg* 2014 Oct;72(10):1938–56.
- [28] Kassebaum NJ, Smith AGC, Bernabé E, Fleming TD, Reynolds AE, Vos T, et al. GBD 2015 Oral Health Collaborators. Global, regional, and national prevalence, incidence, and disability-adjusted life years for oral conditions for 195 countries, 1990–2015: a systematic analysis for the global burden of diseases, injuries, and risk factors. *J Dent Res* 2017 Apr;96(4):380–7.
- [29] Imfeld TN. Identification of low caries risk dietary components. *Monogr Oral Sci* 1983;11:1–198.
- [30] Navazesh M, Kumar SK, University of Southern California School of Dentistry. Measuring salivary flow: challenges and opportunities. *J Am Dent Assoc* 2008;139(Suppl). 355–405.
- [31] Firestone AR, Imfeld T, Schiffer S, Lutz F. Measurement of interdental plaque pH in humans with an indwelling glass pH electrode following a sucrose rinse: a long-term retrospective study. *Caries Res* 1987;21(6):555–8.
- [32] König KG. Karies und Kariesprophylaxe. Goldmann: München; 1971.
- [33] Castro RJ, Maltz M, Arthur RA, Giacaman RA. Anti-caries effect of fluoridated milk-based drink consumed by older adults on an in vitro root caries experimental model. *Arch Oral Biol* 2020 Aug 8;118:104878.
- [34] Moynihan PJ, Kelly SA. Effect on caries of restricting sugars intake: systematic review to inform WHO guidelines. *J Dent Res* 2014;93(1):8–18.
- [35] Gustafsson BE, Quensel CE, Lanke LS, Lundqvist C, Grahnen H, Bonow BE, et al. The Vipeholm dental caries study; the effect of different levels of carbohydrate intake on caries activity in 436 individuals observed for five years. *Acta Odontol Scand* 1954;11(3–4):232–64.
- [36] Geurtsen W, Hellwig E, Klimek J, Beck J, Benz C, Bertzbach F, et al. S2K Guideline (unabridged version). Caries prevention in permanent teeth - basic recommendations 2016. AWMF Register NO.: 083-021. <https://secure.owidi.de/documents/10165/1373255/kariesprophylaxengl.pdf/c20a383e-da66-42bf-862a-9b60c4740054>. [Accessed 1 May 2020].
- [37] Diaz-Garrido N, Lozano C, Giacaman RA. Frequency of sucrose exposure on the cariogenicity of a biofilm-caries model. *Eur J Dermatol* 2016 Jul-Sep;10(3):345–50.
- [38] van Loveren C. Sugar restriction for caries prevention: amount and frequency. Which is more important? *Carbohydr Res* 2019;53(2):168–75.
- [39] Volkert D, Chourdakis M, Faxen-Irving G, Frühwald T, Landi F, Suominen MH, et al. ESPEN guidelines on nutrition in dementia. *Clin Nutr* 2015;34(6):1052–73.
- [40] Industry MNI. Oral nutritional supplements to tackle malnutrition. A summary of the evidence base. Brussels; 2012. https://medical.nutritionindustry.com/files/user_upload/documents/publications/Dossier2012FINAL2012-09-04.pdf. [Accessed 1 May 2020].
- [41] Noonan C, Patrick Noonan W. Marketing dietary supplements in the United States: a review of the requirements for new dietary ingredients. *Toxicology* 2006;221(1):4–8.
- [42] Streicher M, Themessl-Huber M, Schindler K, Sieber CC, Hiesmayr M, Volkert D. nutritionDay in nursing homes – the association of nutritional intake and nutritional interventions with 6-month mortality in malnourished residents. *J Am Med Dir Assoc* 2017;18(2):162–8.
- [43] Castro RJ, Giacaman RA. Dietary supplements for older adults; risk versus benefits for oral health. *J Oral Res* 2018;7(6):228–30.
- [44] WHO. Guideline. Sugars intake for adults and children. Geneva: World Health organization; 2015.
- [45] Giacaman RA. Sugars and beyond. The role of sugars and the other nutrients and their potential impact on caries. *Oral Dis* 2018 Oct;24(7):1185–97.
- [46] BNF 70. BMJ group and the royal pharmaceutical society of great britain [Internet]. 2015. <https://www.bnf.org/wp-content/uploads/2015/08/How-to-use-the-BNF.pdf>. [Accessed 1 May 2020].
- [47] Oral nutritional supplementation and oral health. Recommendations for health care professionals to reduce the impact of oral nutritional supplementation (ONS), sip feeding and nutritional advice on dental health. All Wales Special Interest Group for Special Oral Health Care. 2009. <http://www.sigwales.org/wp-content/uploads/sipfinalcorrectedapril201053.pdf>. [Accessed 21 March 2020].